41

2881

Attorney's Docket No.: 14544-002001 / P61716/003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Philip Marriott	Art Unit	:	2881
Serial No.	:	09/~~787~~,358	Examiner	:	Anthony Quash
Filed	:	May 15, 2001			
Title	:	MEANS FOR REMOVING UNWANTED IONS FROM AN ION TRANSPORT SYSTEM AND MASS SPECTROMETER			

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY TO ACTION OF JUNE 18, 2003

In reply to the Office Action of June 18, 2003, the applicant submits the following remarks.

Claims 1-6 and 8-27 are pending and rejected under 35 U.S.C. § 103(a). The applicant traverses the rejections for the reasons stated below.

1. Rejections under Section 103

a. Rejections over Eiden

Claims 1-5, 13-20 and 27 are rejected as allegedly being unpatentable over U.S. Patent No. 6,259,091 ("Eiden"). The applicant respectfully disagrees, because Eiden fails to disclose or suggest mass spectrometry apparatus or methods in which an initial mass selection of an ion stream and a subsequent mass analysis are performed at the same mass-to-charge ratio.

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

September 18, 2003
Date of Deposit

Signature

Loni M. Cummigns
Typed or Printed Name of Person Signing Certificate

Claim 1 is directed to a mass spectrometer that includes, *inter alia*, a first ion optical device located in a first evacuated chamber for containing an ion beam, a second ion optical device within a collision cell disposed in a second evacuated chamber, and mass-to-charge analyzing means contained within a third evacuated chamber. The first ion optical device is a mass selective device, and the mass-to-charge analyzing means is configured to mass analyze the ion beam to produce a mass spectrum of the ion beam such that both the first ion optical device and the mass-to-charge ratio analyzing means operate at the same mass to charge ratio. Thus, the mass spectrometer includes a mass selective device located before a collision cell, and a mass-to-charge analyzing device located after the collision cell, where the mass selective device and the mass-to-charge analyzing device are configured to operate at the same mass to charge ratio.

The Examiner continues to rely on Eiden, pointing specifically to the disclosure in that reference of a mass spectrometer incorporating a collision cell between a lens stack and a mass analyzer, as illustrated in Figure 7 of Eiden. Pointing to Eiden's definition of the term "ion discriminating unit", the Examiner concludes that Eiden therefore discloses positioning an "ion discriminating unit" before the collision cell. *See* Office Action at page 12. Thus, the Examiner's argument appears to be that: (1) Eiden discloses an arrangement of lens stack, followed by collision cell, followed by mass analyzer; (2) Eiden says lens stacks are "ion discriminating units"; and (3) Eiden therefore discloses an arrangement of a mass selective device, followed by a collision cell, followed by a mass analyzer.

It is important to note, however, that while mass selective devices may fall within the scope of Eiden's "ion discriminating units", not all ion discriminating units are necessarily mass selective. Instead, according to Eiden, "mass analyzer or ion discriminating unit refers to any apparatus which separates charged species according to their m/z *and/or kinetic energy*." *See* Eiden, column 8, lines 47-49 (emphasis added). That is, ion discriminating units, as Eiden uses that term, may include some devices that are mass selective – that is, devices, such as quadrupole ion traps and linear quadrupoles, that separate charged species based on their mass-to-charge ratio. But the term also includes devices that separate charged species based on kinetic energy.

The applicant submits that Eiden's lens stack is at most one such device, and that in any event it does not have the ability to separate ions based on mass-to-charge ratio, as claim 1 requires.

As noted in the previous response, Eiden describes an arrangement in which an ion beam containing analyte ions and carrier gas/matrix ions is created by directing a plasma through two apertures and a lens stack 60. Column 8, lines 35-39. Upon exiting the lens stack 60, the ion beam is directed into an "ion discriminating unit" – quadrupole ion traps and linear quadrupoles are specifically mentioned – from which ions are selectively emitted according to their m/z or kinetic energy and directed to a charged particle detector for detection. *See* column 8, lines 43-49; 59-64; column 9, lines 27, 28. Eiden discloses incorporating a collision cell or ion trap somewhere between the first aperture (i.e., the aperture through which the plasma enters the system) and the charged particle detector. Column 9, lines 17-19; 25-27. More specifically, Eiden notes that a collision cell or an ion trap can be included before the lens stack, between elements of the lens stack, or between the lens stack and the mass analyzer. See column 9, lines 20-25; lines 28-35.

The Examiner focuses on lens stack 750, shown in Figure 7, which is a lens stack that is used in conjunction with a collision cell 710 to replace lens stack 60 of Figures 1, 3 and 4. *See* Eiden, column 15, lines 31-35. As noted in the previous response, Eiden notes that lens stack 60 functions to "focus the ion beam into a narrow stream which is directed to a mass analyser 10 or a linear quadrupole 200 (Figure 3)". *Id.* column 8, lines 43-45. Nowhere, however, does Eiden even hint that lens stack 60 or its replacement 750 have are capable of separating ions based on mass-to-charge ratio. At most, Eiden states that a lens stack can be an "ion discriminating unit". *See* column 8 lines 46-55. But as noted above, this is not the same thing as saying that lens stacks are capable of separating ions based on mass-to-charge.

It is well known in the art that a charged particle that experiences only electrostatic fields does not exhibit any mass dependant effect. As explained in a classic charged particle optics work:

> The equations of motion of a charged particle moving through electrostatic fields can be reduced to differential equations which do not contain either the charge or the mass of the particle.

See Electrostatic Lenses, Harting and Read, Chapter 2, Section 11 (Elsevier, 1976) (copy attached). Since the motion of the particle in an electrostatic field can be described without reference to the particle's mass or charge, it follows that such a field cannot produce a separation of species according to their m/z. Any device that produces such a field cannot act as a mass selective device.

Eiden's disclosure makes it clear that lens stack 60 (and presumably its replacement 750 as well) are operated so as to produce only electrostatic fields. As Eiden explains, "[i]ons are gated into the quadrupole ion trap [which functions as both collision cell and mass analyzer in this embodiment] by switching the potential on lens element 80 in the lens stack 60. The potentials on lens element 80 . . . were switched between a negative value used to admit ions into the quadrupole ion trap, in the range between about –10 V to about –500 V, preferably –35 V, and a positive value used to prevent ions from entering the quadrupole ion trap, in the range between about +10 V to about +500 V, preferably above +10 V, or the kinetic energy of the ions." Eiden, column 10, line 58-column 11, line 1; *see also* column 12, lines 4-27. Thus, according to Eiden, the lens stack is used to generate an electrostatic field in order to gate ions into the collision cell, which cannot result in any mass selective effect as described above.

On the other hand, applying voltages to some of the lens elements in this way to create a gate does make the lens stack 60 function as a crude energy filter, allowing only high energy ions to be admitted into the collision cell. Used in this way, lens stack 60 may act as an "ion discriminating unit", in the sense that it separates charged species based on their energy, but not as a device that separates based on mass-to-charge ratio.

Thus, while Eiden's lens stacks may be "ion discriminating units" in the sense that they can operate to separate charged species based on kinetic energy, nothing in Eiden discloses or suggests the use of such lenses as mass selective devices, to separate ions based on mass-to-charge ratio, as claim 1 requires. And, failing to disclose or suggest a mass selective device located before the collision cell, Eiden necessarily fails to disclose or suggest operating a subsequent mass analyzer at the same mass-to-charge ratio as such an initial mass selective device. Because Eiden thus fails to disclose or suggest at least these limitations of claim 1, the

applicant submits that no *prima facie* showing of obviousness has been made, and asks that claim 1 be allowed.

Claims 2-5 are dependent claims based on claim 1, and therefore necessarily include all limitations of that claim. Claims 13-20 are method claims that analogously include the steps of mass selecting an ion beam at an analyte mass to charge ratio, transmitting at least a portion of the mass selected ion beam into a collision cell, and mass analyzing the ion beam in a mass analyzer at the same analyte mass to charge ratio. Claim 27 is an apparatus claim that includes limitations directly analogous to the limitations discussed above in the context of claim 1. The applicant submits that all of these claims are allowable over Eiden for at least the reasons discussed above in the context of that claim.

b. Rejections over Eiden and Tanner

Claims 6, 8-11, 21-24 and 26 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Eiden in view of U.S. Patent No. 6,140,638 ("Tanner"). Claims 6 and 8-11 are dependent claims derived from claim 1, and therefore include all limitations of that claim. Claims 21-24 and 26 are dependent claims derived from claim 13, and similarly include all of the limitations of that claim.

As discussed above, Eiden fails to disclose or suggest methods or apparatus in which a mass selection step is performed on an ion beam prior to introduction into a collision cell, and in which a subsequent mass analysis step is performed at the same mass-to-charge ratio as the initial mass selection. Tanner appears to be equally lacking, disclosing instead a system in which a mass selection is performed in the collision cell itself. *See* Abstract. Accordingly, claims 6, 8-11, 21-24 and 26 are allowable over the combination of Eiden and Tanner for at least the reasons discussed above with respect to claim 1.

c. Rejections over Eiden and Okamoto

Claims 12 and 25 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Eiden in view of U.S. Patent No. 5,049,739 ("Okamoto"). Claims 1 and 25 are dependent claims based on claims 1 and 13, respectively, and include all of the limitations of their parent claims.

As discussed above, Eiden fails to disclose or suggest methods or apparatus in which a mass selection step is performed on an ion beam prior to introduction into a collision cell, and in which a subsequent mass analysis step is performed at the same mass-to-charge ratio as the initial mass selection. Okamoto, which appears to disclose nothing more than the use of a collision cell, is equally lacking. Accordingly, claims 12 and 25 are allowable over Eiden and Okamoto for at least the reasons discussed above in the context of claim 1.

2. Conclusion

The applicant submits that all claims are in condition for allowance and asks that all claims be allowed. No fees are believed to be due at this time. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 9/18/03

Timothy A. Porter
Reg. No. 41,258

Fish & Richardson P.C.
500 Arguello Street, Suite 500
Redwood City, California 94063
Telephone: (650) 839-5070
Facsimile: (650) 839-5071

50174608.doc

ELECTROSTATIC LENSES

BY

E. HARTING

Senior Lecturer in Physics,
The University of New South Wales,
Australia.

AND

F. H. READ

Professor of Physics,
University of Manchester,
England.

With Contributions by J.N.H. Brunt

ELSEVIER SCIENTIFIC PUBLISHING COMPANY
Amsterdam - Oxford - New York 1976

ELSEVIER SCIENTIFIC PUBLISHING COMPANY
335 JAN VAN GALENSTRAAT
P.O. BOX 211, AMSTERDAM, THE NETHERLANDS

AMERICAN ELSEVIER PUBLISHING COMPANY, INC.
52 VANDERBILT AVENUE
NEW YORK, NEW YORK 10017

Library of Congress Cataloging in Publication Data

Harting, E
Electrostatic lenses.

Includes bibliographical references and index.
1. Electrostatic lenses. I. Read, Frank Henry, joint author. II. Brunt, J. N. H., joint author. III. Title. [DNLM: 1. Lenses. 2. Spectrum analysis--Instrumentation. QC454 H329e]
QC544.E5H37 537.2'028 75-35792
ISBN 0-444-41319-7

With 37 illustrations and 34 tables

Printed in The Netherlands

LIST OF CONTENTS

and

$$F = -0.25M^4 f_1^{-3}(4C_{s0} + M^{-1}C_{s1} - 1.5f_1 M^{-1}) \quad \text{(II.28)}$$

when the reference plane is taken to be the first focal plane. The coefficient A is related to the spherical aberration coefficient by [1]:

$$A = |M|(P - F_1)^{-3} C_s = M^4 f_1^{-3} C_s \qquad \text{(II.29)}$$

and it can be seen that this relationship is indeed consistent with the previous definitions of A and C_s. The coefficients B, C, D and F are the coefficients of astigmatism, field curvature, coma and distortion, respectively [1].

Equations II.19 and II.29 also apply, with the appropriate change from C_s to C, to lenses of planar symmetry.

11. Ion lenses

The equations of motion of a charged particle moving through electrostatic fields can be reduced to differential equations which do not contain either the charge or the mass of the particle (see Chapter VI, section 2). The data for electrostatic lenses therefore apply not only to non-relativistic electrons, but equally well to non-relativistic negative or positive ions, the only difference being that the signs of all the applied voltages are reversed in the case of positively charged particles.

2. Integration of the paraxial ray equation to obtain focal and mid-focal lengths

The equations of motion of a charged particle travelling near the axis of a cylindrically symmetric system can be reduced in the non-relativistic limit to the paraxial ray equation [1, 2, 3]

$$\frac{d^2r}{dz^2} + \frac{\phi'}{2\phi}\frac{dr}{dz} + \frac{\phi''}{4\phi}r = 0 \qquad \text{(VI.10)}$$

where (r,z) is the path of the particle. Note that this equation does not contain the charge or mass of the particle, as noted in Chapter II, section 11. Equation VI.10 can be further reduced to the Pichet equation

$$\frac{d^2\rho}{dz^2} + \frac{3}{16}\left(\frac{\phi'}{\phi}\right)^2 \rho = 0 \qquad \text{(VI.11)}$$

where $\rho = r\phi^{1/4}$. The analogous equation for lenses of planar symmetry is

$$\frac{d^2\rho}{dz^2} + \left\{\frac{3}{16}\left(\frac{\phi'}{\phi}\right)^2 + \frac{\phi''}{4\phi}\right\}\rho = 0 \qquad \text{(VI.12)}$$

where $\rho = x\phi^{1/4}$ and the path of the particle is (x,z).

In the programs which we have constructed and used the functions ϕ are found as described in section 1 above, and then ϕ' is calculated by numerical differentiation, and the function

$$T(z) = \phi'(z)/\phi(z) \qquad \text{(VI.13)}$$

and its derivative $T'(z)$ are calculated. In terms of T and T', equations VI.11 and VI.12 become

$$\rho'' + \frac{3}{16}T^2\rho = 0 \qquad \text{(VI.14)}$$

and

$$\rho'' + \left(\frac{7}{16}T^2 + \frac{1}{4}T'\right)\rho = 0 \qquad \text{(VI.15)}$$

respectively. These equations are integrated numerically by the Fox-Goodwin method. Two integrations with different initial conditions are carried out for each lens to obtain two independent ray trajectories $r_1(z)$ and $r_2(z)$.

The general solutions of the second order equations VI.14 and VI.15 are linear combinations of any two independent solutions, and therefore any general paraxial ray $r(z)$ passing through the lens must be a linear combination of r_1 and r_2, that is

$$r(z) = \alpha r_1(z) + \beta r_2(z) \qquad \text{(VI.16)}$$

By choosing α and β in such a way that $r(z)$ is initial-